Transmission of HTLV-I and –II by Blood Transfusion

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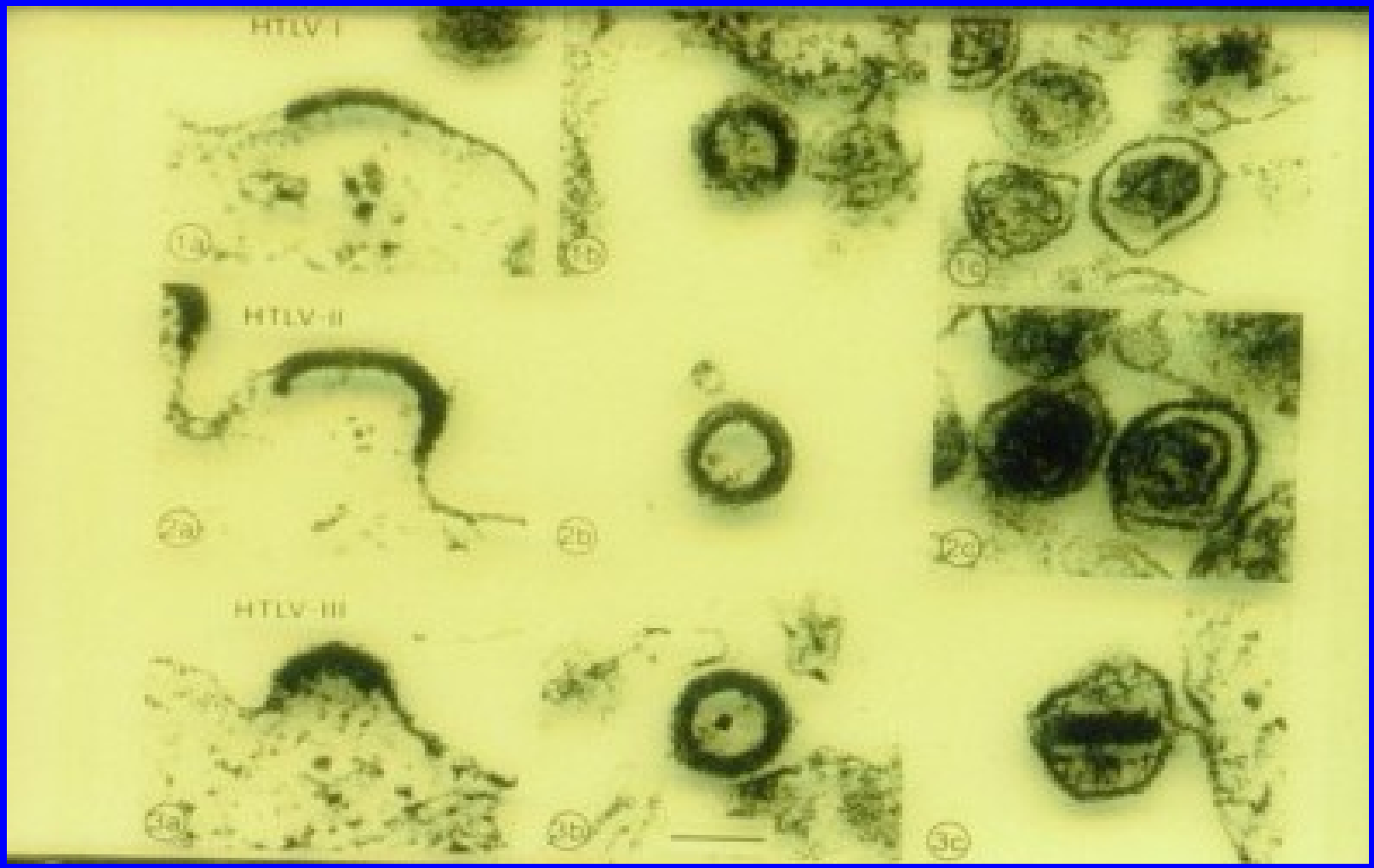
Outline

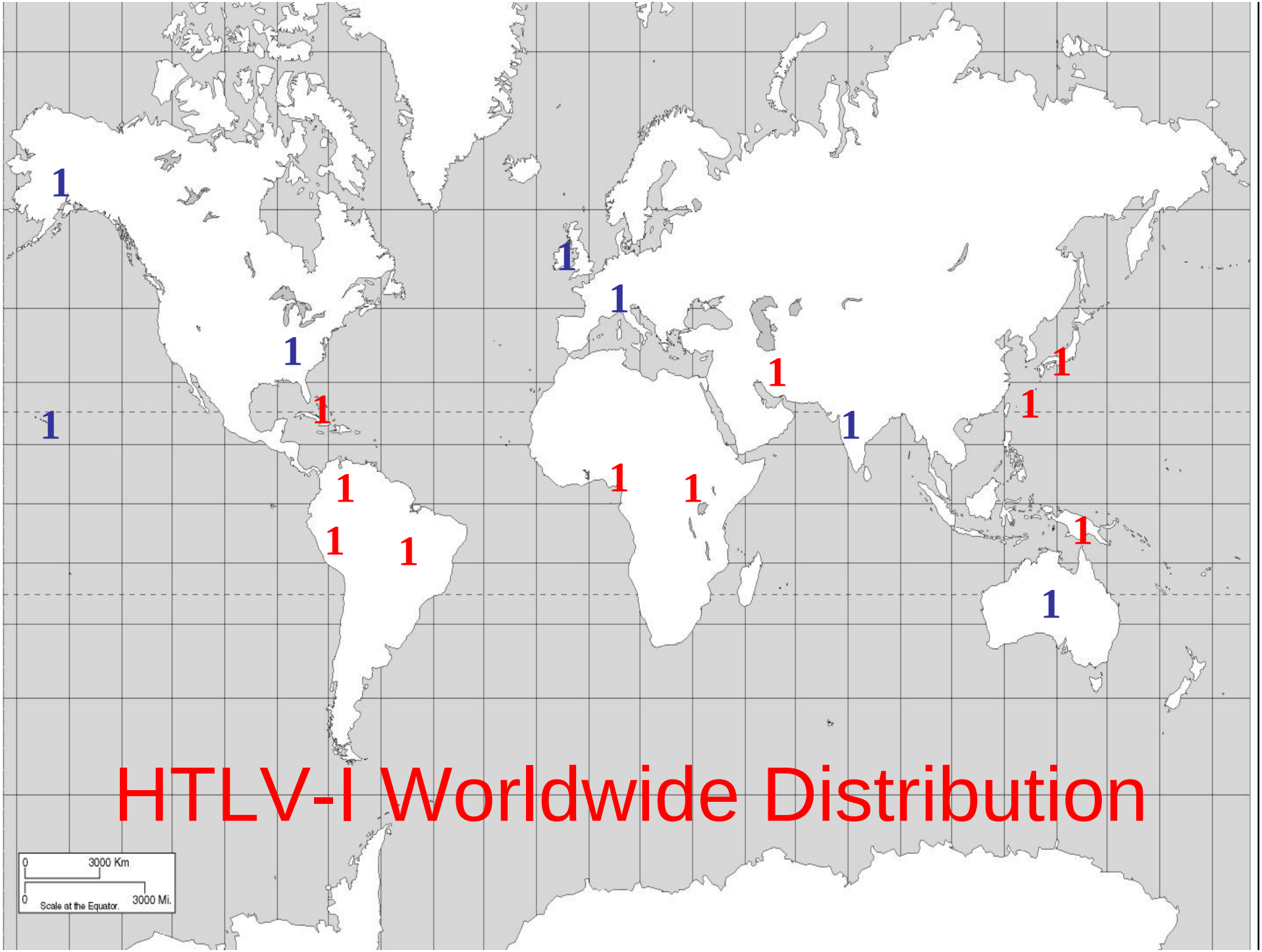
- Background on HTLV
- HTLV disease outcomes
- Transmission by blood transfusion
- Prevalence and risk groups
- Incidence
- Conclusions & recommendations

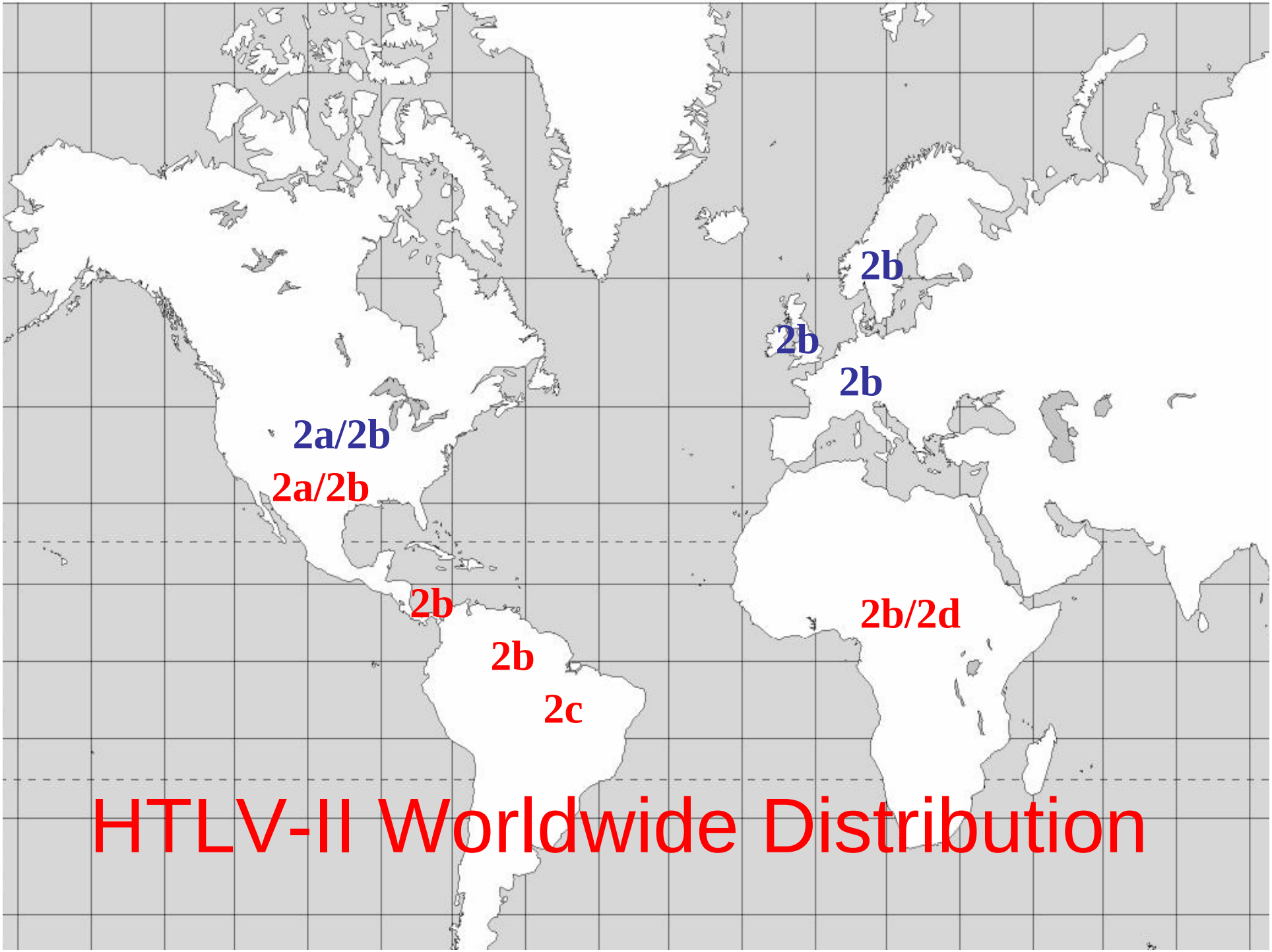
HTLV-I, HTLV-II and HIV



Background on HTLV

- Deltaretrovirus, related to bovine leukemia virus, only remotely to HIV (lentivirus)
- Likely simian origin, but ancient (>15,000 years) infection of humans
- Chronic infection = integrated provirus, little free virus production, cell-to-cell infection, inoculation with infected cells
- Worldwide, but spotty distribution


HTLV-I Worldwide Distribution
0 3000 Km
0 3000 Mi.
Scale at the Equator.

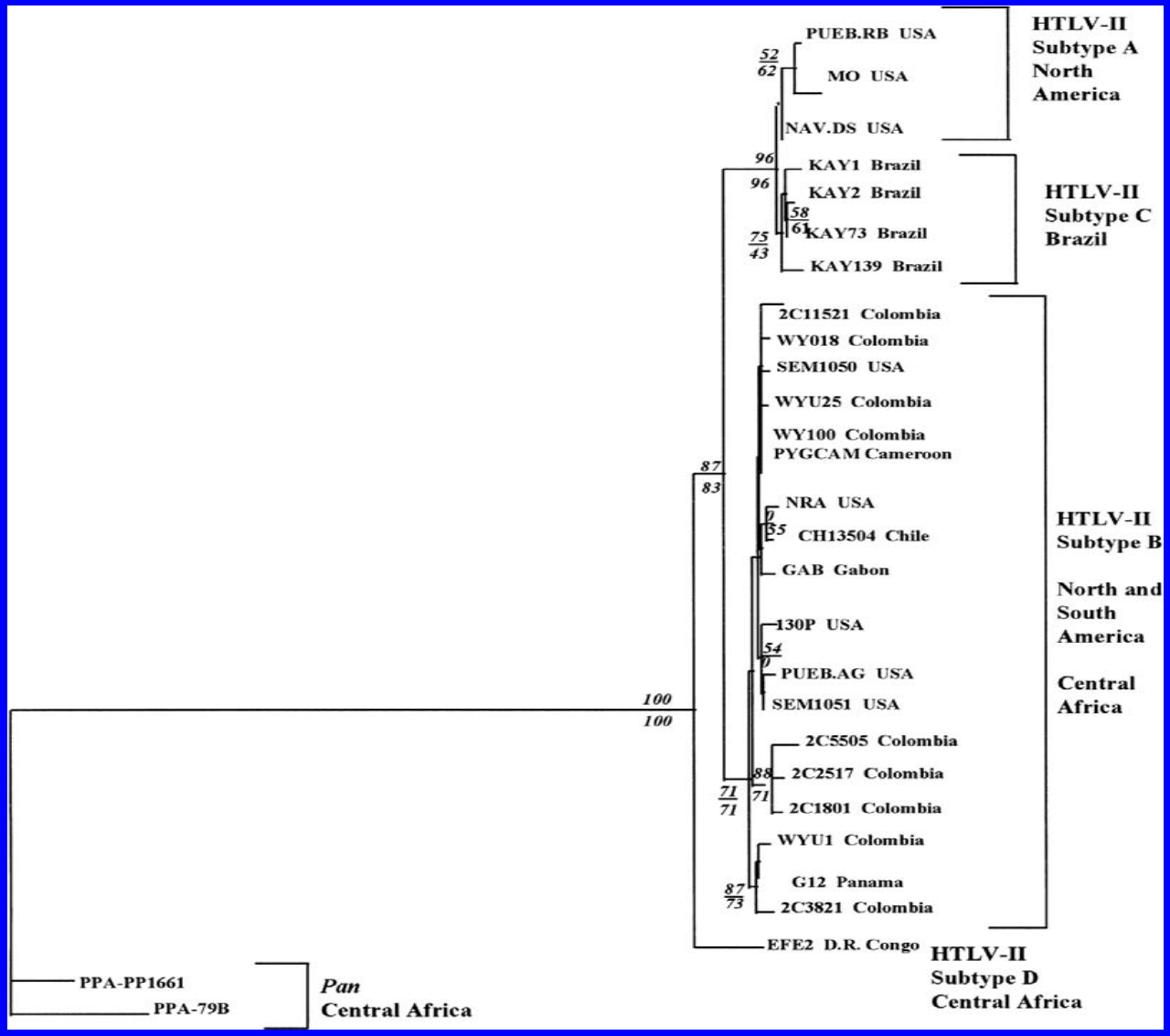

2b
2b
2b
2a/2b
2a/2b
2b
2b
2c
2b/2d
HTLV-II Worldwide Distribution

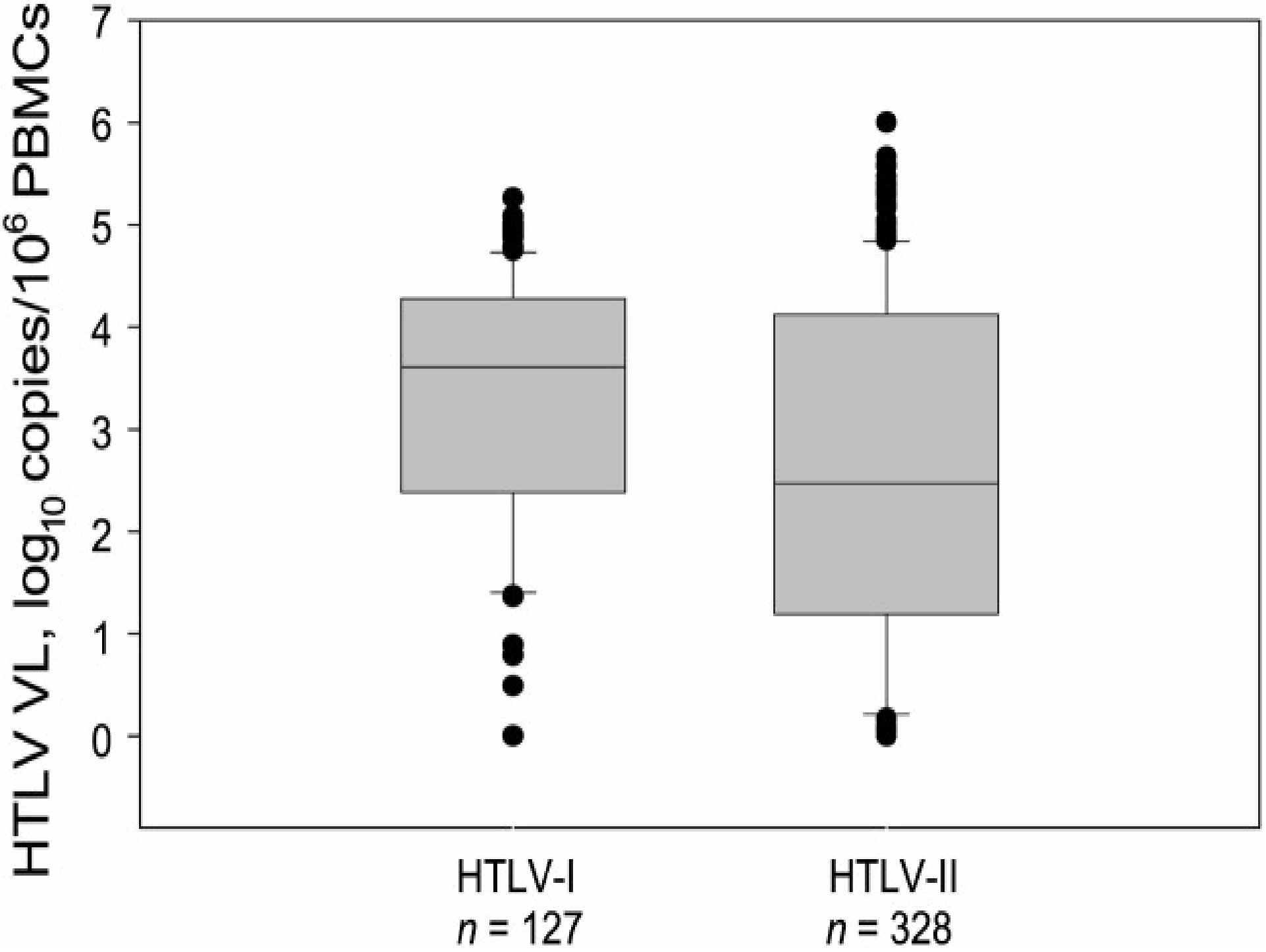
HTLV and STLV Phylogeny

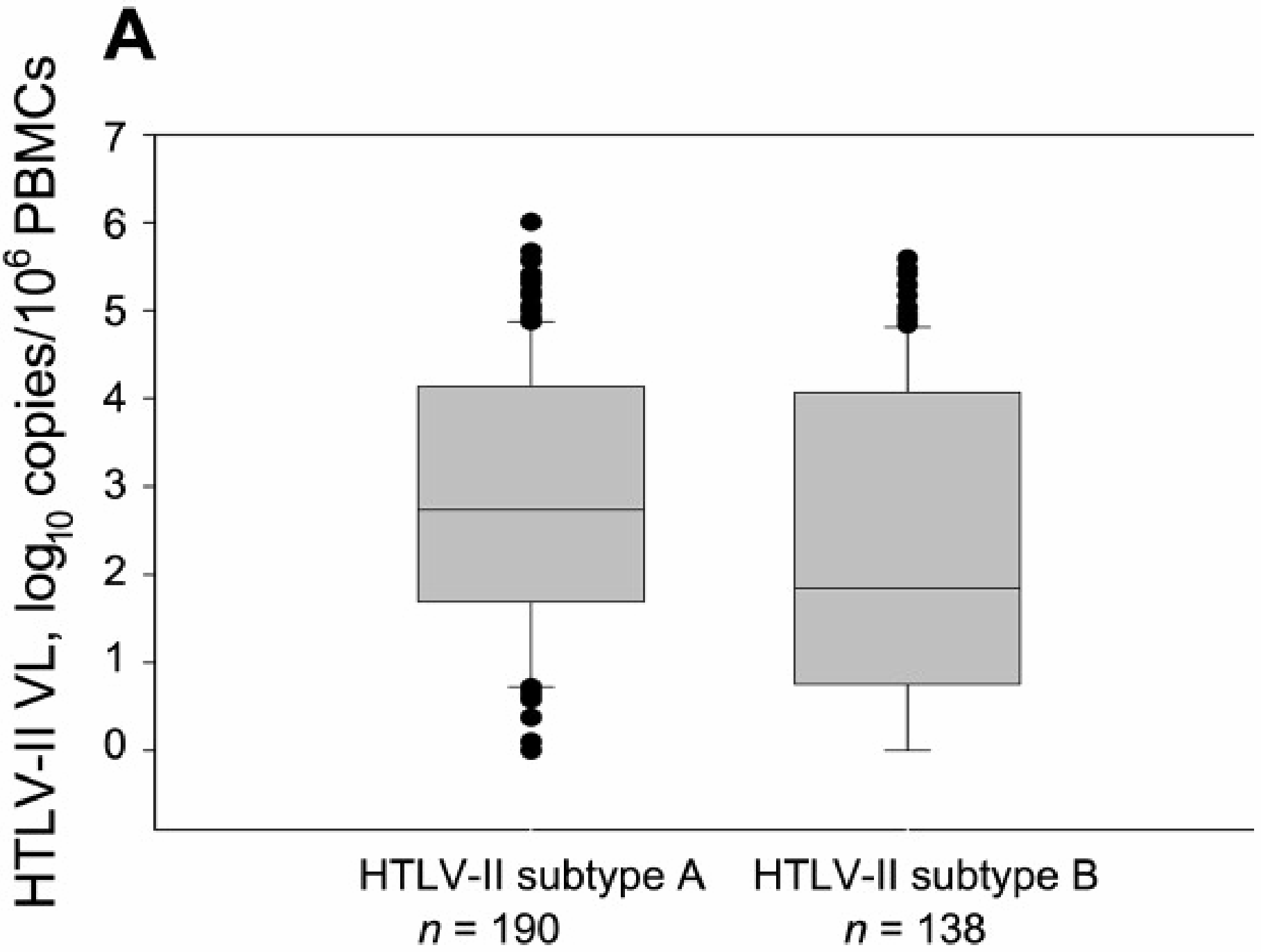
452 bp env gene

HTLV-II Phylogeny (excluding IDU)

417 bp LTR region




HTLV VL, log10 copies/10^6 PBMCs
7
6
5
4
3
2
1
0
HTLV-I
n = 127
HTLV-II
n = 328


A
HTLV-II VL, log10 copies/10^6 PBMCs
7
6
5
4
3
2
1
0
HTLV-II subtype A
n = 190
HTLV-II subtype B
n = 138

HTLV diseases

- HTLV-I
  - Adult T-cell leukemia (ATL); 2-4% attack rate
  - HTLV-assoc myelopathy (HAM/TSP); 2% attack rate
  - Uveitis
  - ? Arthritis and other autoimmune diseases
- HTLV-II
  - HAM/TSP; 1% attack rate
  - ? Pneumonitis and bronchitis
  - ? Arthritis
  - Increased mortality

HTLV-I and –II Transmission by Blood

- HTLV-I transmission (Okochi *Vox Sang* 1984)
  - WB or PRBC: 26/41 (63%) seroconverted
  - FFP: 0/14 (0%) seroconverted
  - HTLV NEG 0/252 (0%) seroconverted
- Cases of both ATL and HAM following transfusion-acquired HTLV-I

HTLV-I Transmission by Blood

Manns et al. *Int J Cancer* 1992

- HTLV-I transmission rate & window period:
  - WB, PRBC, Plat: 24/54 (44%) 51 days
  - FFP, Cryo: 0/12 (0%) ----

- Storage time*:

	0-6d	7-14d	15+d
Transmission	20	5	0
Non-Transm	11	14	5

* p=0.0008

HTLV-I and –II Transmission by Blood

Donegan *Transfusion* 1994

- PRBC or PLT: 26/54 (35%)
  FFP. Cryo, Frozen 0/21 (0%)

- HTLV-I 9/17 (53%)
  HTLV-II 17/57 (30%)

- Storage time*:

	0-5d	6-10d	11-14d
Transmission	17	8	0
Non-Transm	6	10	10

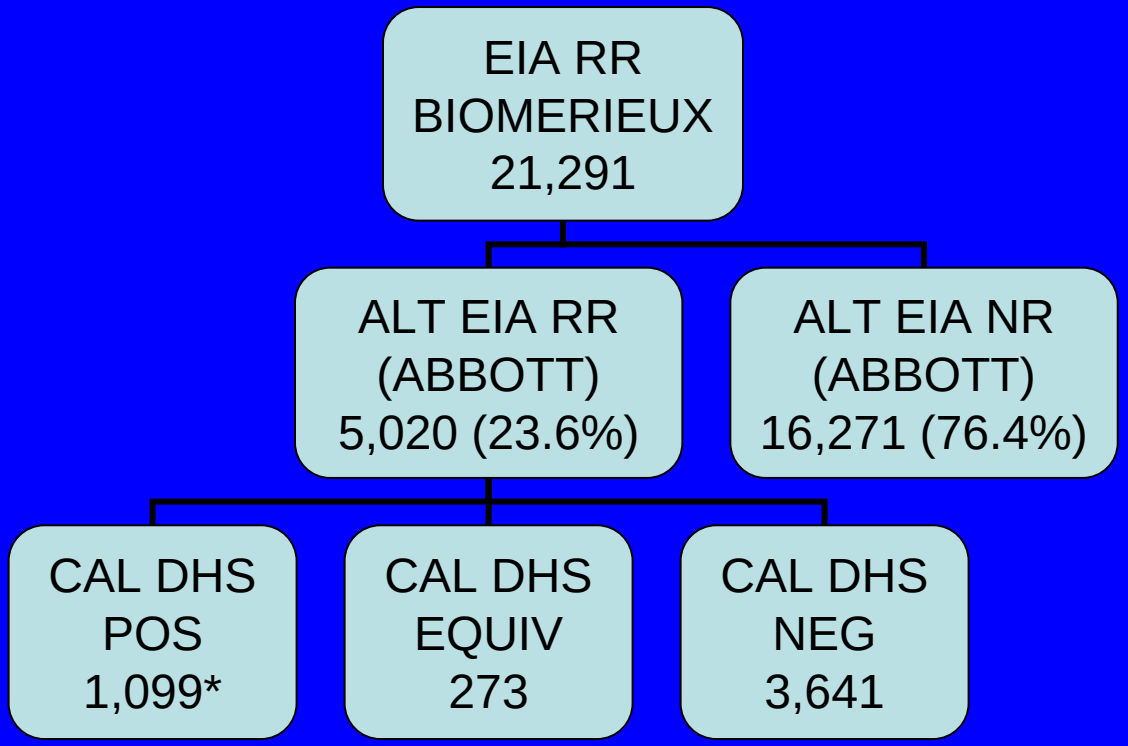
* p=0.0002

Current Blood Testing for HTLV

- Screen EIA: Ortho/Biomerieux
  - HTLV-I and –II virus lysate
- ALT EIA: Abbott
  - HTLV-I and –II virus lysate
- No licensed supplemental test!
- California DHS lab supplemental testing
  - In-house IFA, Western blot, RIPA

ARC HTLV-I/II Prevalence

17.2 million donations MAR02-DEC04



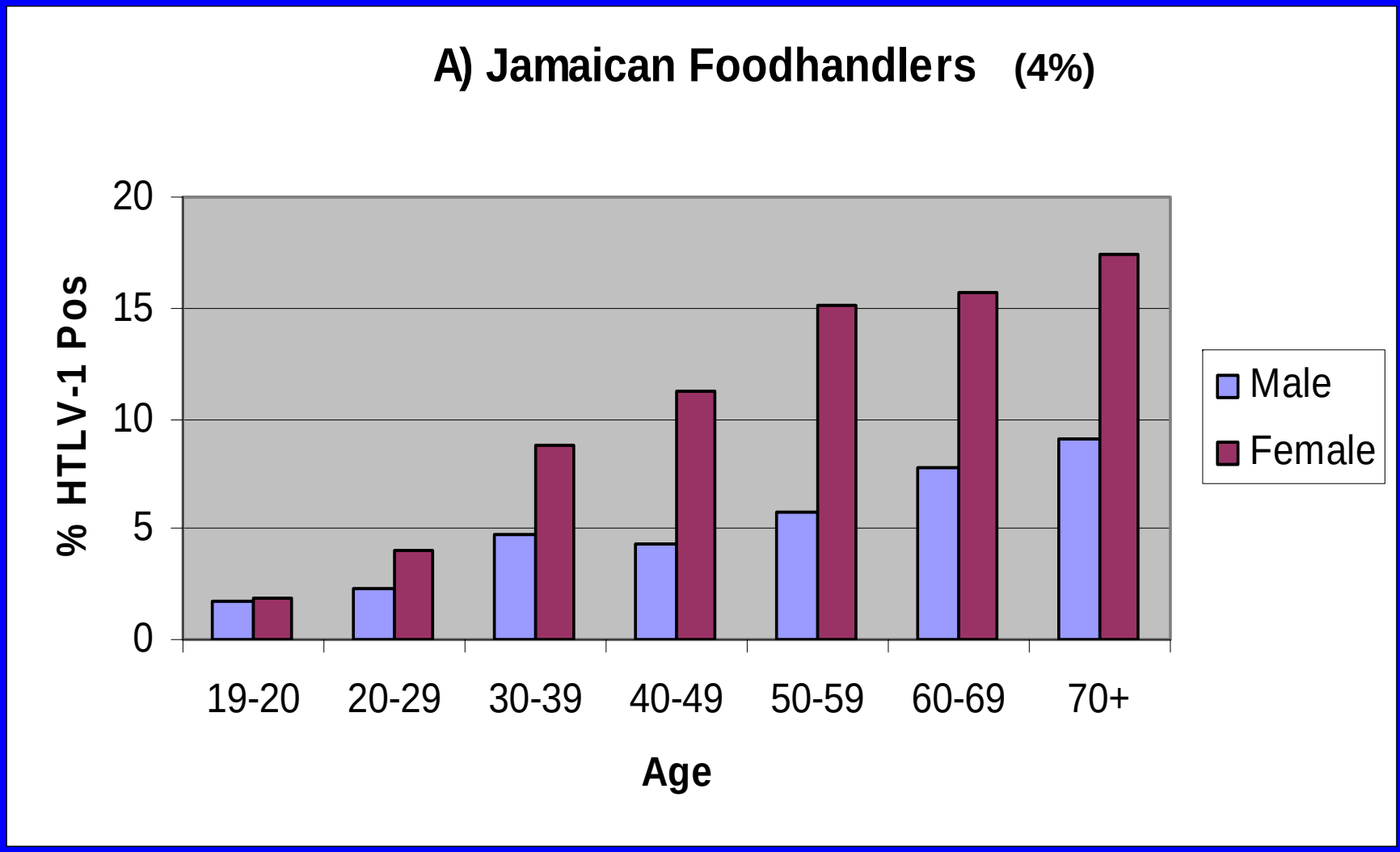
* 0.64 per 10,000 donations; 5.2% of initial EIA RR's

EIA Sensitivity to HTLV-II

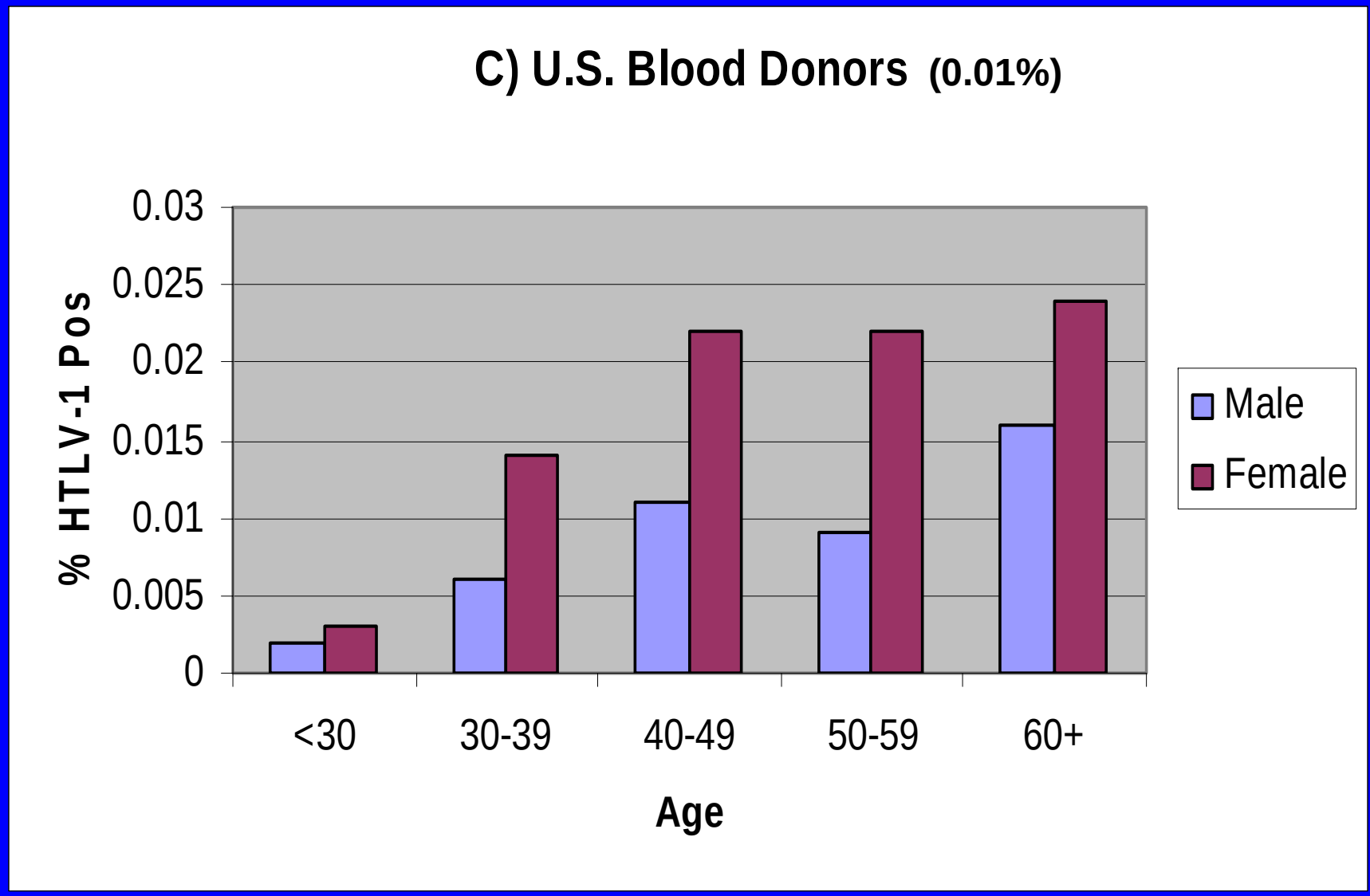
- Liu Transfusion 1999 (USA IDU)
  - Camb Biotech EIA 530/557 (95.1%)
  - Abbott 7A92 EIA 554/557 (99.5%)
  - Roche PCR 474/557 (85.1%)

  (but 47 (7.5%) PCR+ among 627 NEG on all EIA's)
- Poiesz Transfusion 2000 (IDU & S. Amer Indian)
  - Vironostika HTLV-I and –II 144/204 (71%)
  - Camb Biotech HTLV-I + rgp21 155/204 (76%)
  - Abbott HTLV-I and –Iib 159/204 (78%)
  - HTLV-II research PCR 200/204 (98%)

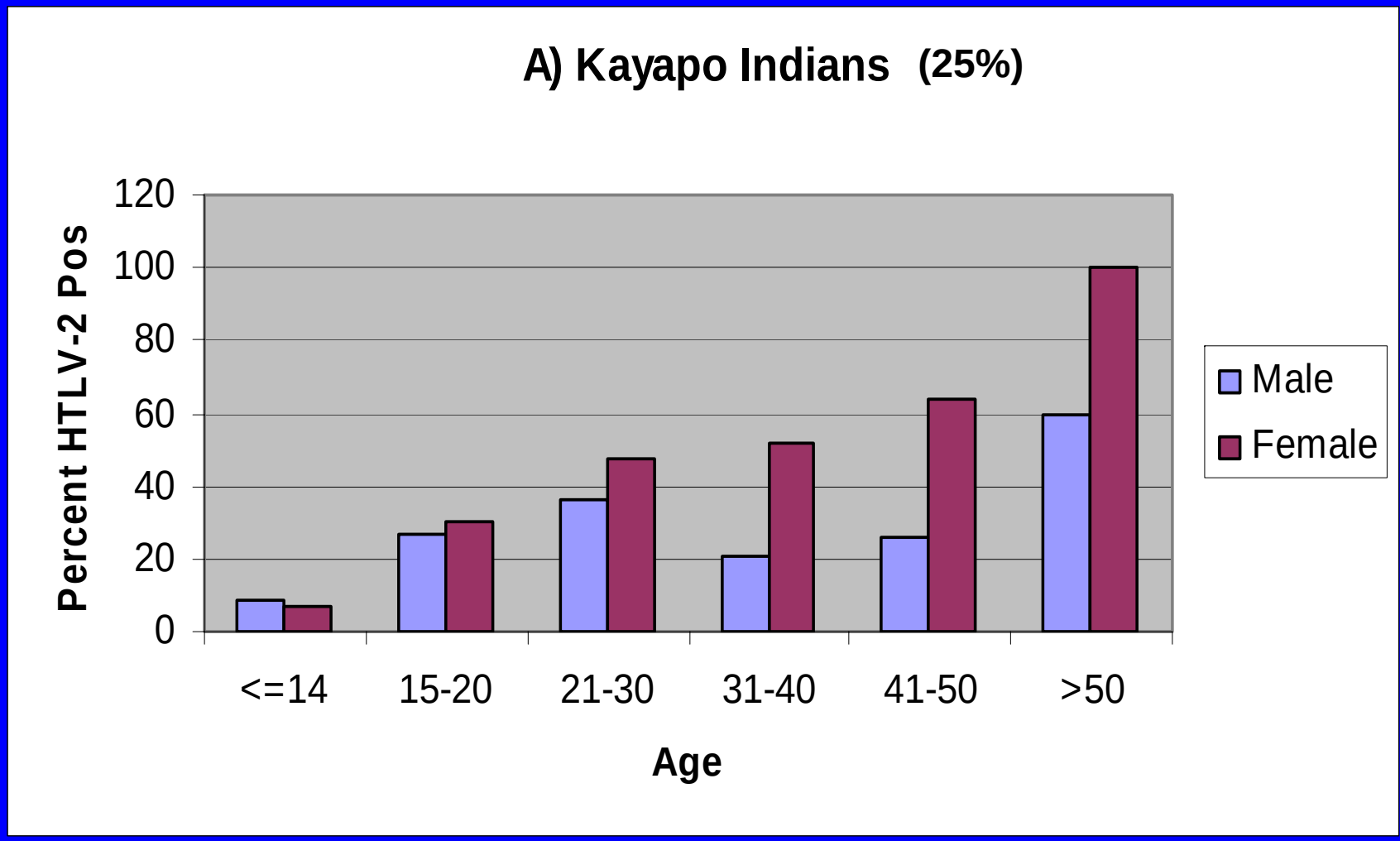
HTLV-I Prevalence



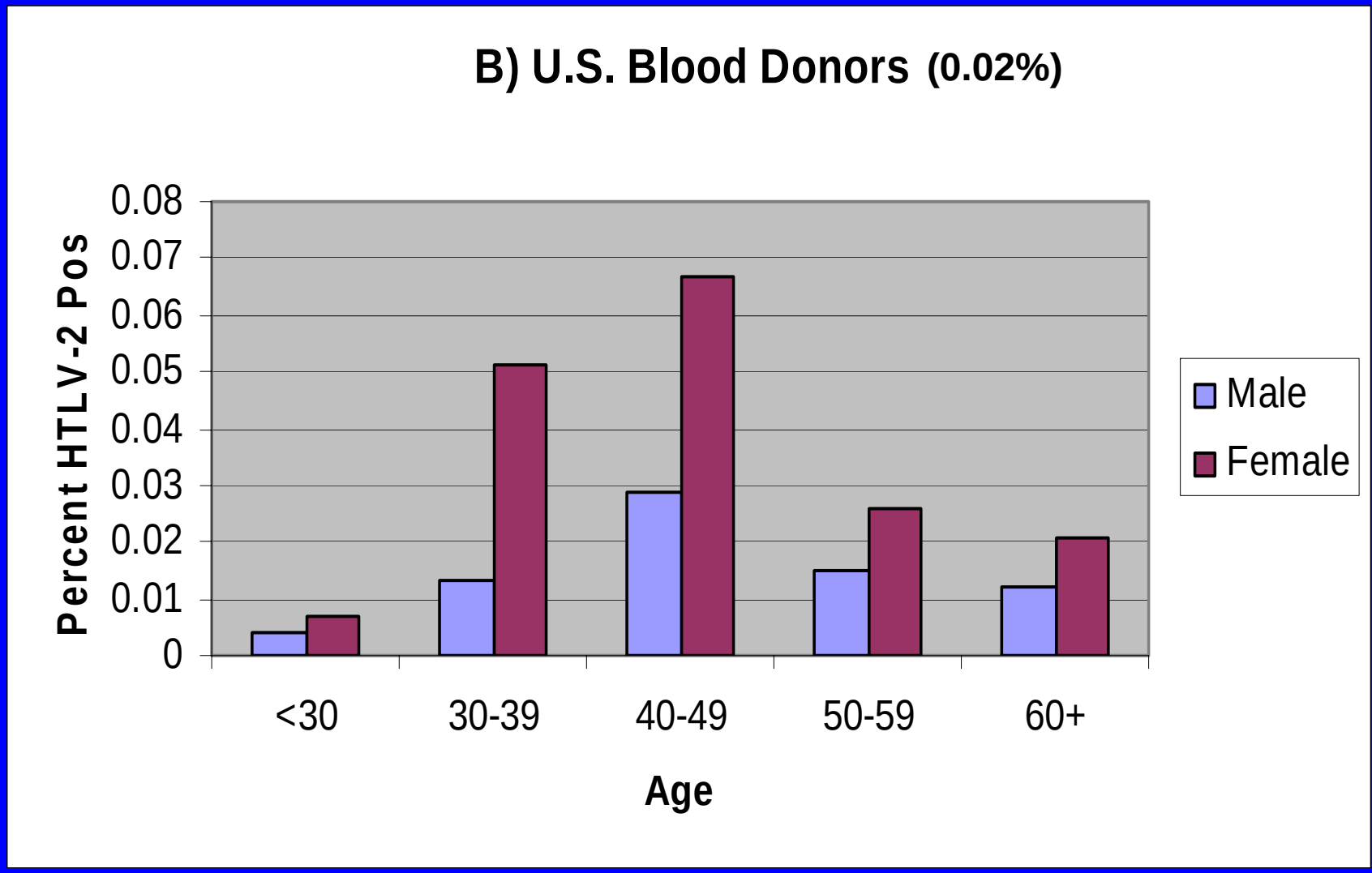
HTLV-I Prevalence



HTLV-II Prevalence



HTLV-II Prevalence



HTLV Risk Groups - USA

HTLV-I

- Japanese American, Caribbean, Central African ethnicity: 0.1% to 1%
- Prostitutes (7%), STD clinics (0.4%)

HTLV-II

- IDU: 0.5% to 17.6%, by city
- Sex partner of IDU: ~0.5%
- Native American: 2% - 3%

HTLV-I and –II Risk Factors

Schreiber *JAIDS* 1997; Murphy *JID* 1999

	Approx OR
• HTLV-I	
– <= HS Educ, minority race	5-10
– Hx blood transfusion	6
– >= 7 lifetime sex parts	3
– Endemic sex partner	2
• HTLV-II	
– Sex partner IDU	20
– Self IDU	10
– <= HS educ, minority race	5-10
– >= 7 lifetime sex parts	3

Incidence of HTLV-I and –II

U.S. blood donors

- Schreiber *NEJM* 1996
  - 1991-93: 9 serocon/ 801,572 P-Y
  - Incidence = 1.12 (0.51-1.98) per 10^5 P-Y
  - Resid risk = 1.56 (0.50-3.90) per 10^6 units
- Glynn *JAMA* 2000
  - 1991-96; 2-5 incident cases per year
  - Incidence = 1.59 (1.12-2.19) per 10^5 P-Y
  - Slight but NS increase over six years studied

ARC HTLV-I/II Incidence 1999-2004

- 38 seroconverting donors,
  - 12 HTLV-I, 12 HTLV-II, 14 untypable
- mean inter-donation interval in seroconverters = 966 days
- Incidence = 1 per 737,000 repeat donors, or ___ per 10^6 person-years (???)

HTLV-I and –II Residual Risk

- Has not been estimated since Schreiber NEJM 1996
- Probably still 1-2 per million units
- Cold storage and leukoreduction probably reduce risk but inferential data only

Conclusions

- Prevalent HTLV-I and -II concentrated in sex partners of IDU, sexually active, low education and minority race/ethnicity popns
- Current HTLV-I/II EIA's may lack sensitivity to HTLV-II; no licensed supplemental assay
- Current HTLV residual risk is unclear:
  - incidence may still be higher than HIV or HCV
  - cold storage and leukoreduction effects unclear

Recommendations

- Maintain lifetime deferral for IDU; consider same for sex with IDU
- Research on current EIA sensitivity
- “Orphan” licensure of HTLV supplemental serologic assay…..or
- Addition of HTLV-I and –II NAT once cellular sample prep available